Update on clinical trials at OHSU
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Complete clinical trials

- PAIN-CONTRoLS: Patient Assisted Intervention for Neuropathy: Comparison of Treatment in Real Life Situations
- Phase 3, Multi-National, Double-Blind, Randomized, Placebo-Controlled, Stratified, Parallel Group Study to Evaluate the Safety, Tolerability and Efficacy of Tirasemtiv in Patients with Amyotrophic Lateral Sclerosis (ALS)
- Phase 2 Study of Rasagiline for Treatment of Amyotrophic Lateral Sclerosis
- A randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety and efficacy of ecuizumab in subjects with refractory generalized Myasthenia Gravis (gMG)

Patient Assisted Intervention for Neuropathy: Comparison of Treatment in Real Life Situations (PAIN-CONTRoLS)

- **Objective:** To determine which of the 4 pharmaceutical therapies (pregabalin, duloxetine, nortriptyline or mexiletine) is most effective for neuropathic pain and best tolerated in cryptogenic sensory polyneuropathy (CSPN).

- **Results:** There were a total of 402 CSPN patients with 134, 126, 73, and 69 randomized to nortriptyline, duloxetine, pregabalin, and mexiletine, respectively. The posterior probability each treatment was best were 0.52, 0.43, 0.05, and 0.00, with efficacy rates 25.4%, 23.0%, 15.1%, 20.3% and quit rates of 38.1%, 37.3%, 42.5%, 58.0%, respectively.

- **Conclusions:** Mexiletine met our criteria for being a loser, primarily due to side effects. While there was no clear winner, overall nortriptyline and duloxetine outperformed pregabalin and mexiletine.

A randomized, double-blind, placebo-controlled, multi-center study to evaluate the safety and efficacy of ecuizumab in subjects with refractory generalized Myasthenia Gravis (gMG)

- **Objective:** to determine safety and efficacy of ecuizumab (C5 complement inhibitor) in GMG

- **Results:** 62 with ecuizumab and 63 with placebo. The primary analysis showed no significant difference between ecuizumab and placebo (least-squares mean rank 56.6 [4.5] vs 68.3 [4.5]). Myasthenia gravis exacerbations were reported by six (10%) patients in the ecuizumab group and 15 (24%) in the placebo group. Six (10%) patients in the ecuizumab group and 12 (19%) in the placebo group required rescue therapy.

- **Conclusion:** The change in the MG-ADL score was not statistically significant between ecuizumab and placebo, as measured by the worst-rank analysis. Ecuizumab was well tolerated. The use of a worst-rank analytical approach proved to be an important limitation of this study since the secondary and sensitivity analyses results were inconsistent with the primary endpoint results; further research into the role of complement is needed.
Phase 2 Study of Rasagiline for Treatment of Amyotrophic Lateral Sclerosis

• FINDINGS: Between July 2, 2013, and Nov 11, 2014, 273 patients were screened for eligibility, and 252 patients were randomly assigned to receive rasagiline (n=127) or placebo (n=125). 126 patients taking rasagiline and 125 taking placebo were included in the intention-to-treat analysis. For the primary outcome, the survival probability at the end of the study was 0.43 (95% CI 0.25–0.59) in the rasagiline group (n=126) and 0.53 (0.43–0.62) in the placebo group (n=125). The estimated effect size (hazard ratio) was 0.91 (one-sided 97.5% CI: 0.64–1.34; p=0.31). Rasagiline was well tolerated, and most adverse events were due to amyotrophic lateral sclerosis disease progression rather than treatment; the most frequent of these were dysphagia (32 [25%] taking rasagiline vs 24 [19%] taking placebo) and respiratory failure (25 [20%] vs 31 [25%]). Frequency of adverse events were comparable between both groups.

• INTERPRETATION: Rasagiline was safe in patients with amyotrophic lateral sclerosis. There was no difference between groups in the primary outcome of survival, although post-hoc analysis suggested that rasagiline might modify disease progression in patients with an initial slope of Amyotrophic Lateral Sclerosis Functional Rating Scale Revised greater than 0.5 points per month at baseline. This should be confirmed in another clinical trial.

A Phase 3, Multi-National, Double-Blind, Randomized, Placebo-Controlled, Stratified, Parallel Group, Study to Evaluate the Safety, Tolerability and Efficacy of Tirasemtiv in Patients with Amyotrophic Lateral Sclerosis (ALS)

• Tirasemtiv, a selective fast skeletal muscle troponin activator, as a potential treatment for patients with amyotrophic lateral sclerosis: study design and baseline characteristics.

• Primary Outcome Measures:
  - Change from baseline to Week 24 of the double-blind, placebo-controlled phase in percent predicted slow vital capacity (SVC) [Time Frame: 24 weeks]

• An imbalance of non-serious adverse events (mostly lightheadedness or dizziness) contributed to an imbalance of treatment withdrawals from the clinical trial which confounded the assessment of a potential therapeutic effect for tirasemtiv vs. placebo.

BMY338 (bimagrumab) in patients with sporadic inclusion body myositis

• Bimagrumab is a human monoclonal antibody that binds to type II activin receptors and prevents the binding of its ligands (e.g., myostatin, activin A). These ligands normally act as inhibitors of muscle growth and protein anabolism; bimagrumab lifts this inhibition and can increase muscle mass in young and older adults.

• Change From Baseline in 6 Minute Walking Distance (6MWD) Test at Week 52

Completed EAPs

• Expanded access protocol of Patisiran for patients with hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) with polyneuropathy

• 3,4-Diaminopyridine for Lambert-Eaton Myasthenic Syndrome (still ongoing for Musk + MG and Congenital Myasthenia) Source: Jacobus Pharmaceutical Company Inc

• Expanded Access Program for Inotersen (ISIS 420915) in Patients With Hereditary Transthyretin Amyloidosis (hATTR)
Clinical trials ongoing (1/3)

- Evaluation of the safety, tolerability, efficacy and activity of AMX0035, a fixed combination of Phenylbutyrate (PB) and Tauroursodeoxycholic Acid (TUDCA), for treatment of amyotrophic lateral sclerosis (ALS)
- Genomic Translation for ALS Clinical care (GTAC)
- CY 5022: A Phase 2, Multi-Center, double-blind, randomized, dose-ranging, placebo-controlled study to evaluate the efficacy, safety, and tolerability of CK-3127107 in patients with amyotrophic lateral sclerosis (ALS)
- Effects of oral levosimendan (ODM-109) on respiratory function in patients with ALS
- BIOS: Fluid Biomarkers with Deep Phenotyping in Patients with ALS

Clinical trials ongoing (2/3)

- A Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase 3 Trial to Evaluate the Efficacy, Safety and Tolerability of ARGX-113 in Patients with Myasthenia Gravis Having Generalized Muscle Weakness (ADAPT)
- A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of ACE-083 in Patients with Facioscapulohumeral Muscular Dystrophy
- A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study of ACE-083 in Patients with Charcot-Marie-Tooth Disease Types 1 and X
- HELIOS-A: A Phase 3 Global, Randomized, Open-label Study to Evaluate the Efficacy and Safety of ALN-TTRSC02 in Patients with Hereditary Transthyretin Amyloidosis (NATTR Amyloidosis)
- A Phase 1, Open-label, Dose Escalation Study of Intravenous PRX004 in Subjects with Amyloid Transthyretin (ATTR) Amyloidosis

Clinical trials ongoing (3/3)

- A phase 3 randomized, multicenter, multinational, double-blinded study comparing the efficacy and safety of repeated biweekly infusions of neoGAA (GZ402666) and alglucosidase alfa in treatment-naive patients with late onset Pompe disease
- A Multi-Center, Low Interventional Study with a Retrospective Component in Participants with Late Onset Pompe Disease
- A Phase 3 Double-Blind Randomized Study to Assess the Efficacy and Safety of Intravenous ATB200 Co-Administered with Oral AT2221 in Adult Subjects with Late-Onset Pompe Disease Compared with Alglucosidase Alfa/Placebo
- Prospective, Double-blind, Randomized, Placebo-Controlled Phase III Study Evaluating Efficacy and Safety of Octagam 10% in Patients With Dermatomyositis (“PRODERM study”) (GAM10-08)

ACE-083
Efgartigimod blocks FcRn, leading to IgG elimination

- Efgartigimod is a human IgG1 Fc fragment that targets and blocks specifically to FcRn, blocking the recycling of IgG, leading to the elimination of IgG antibodies.
- Efgartigimod is engineered to bind with high affinity for FcRn.
- Novel MOA for treating MG by targeting IgG antibodies, including AChR & MuSK antibodies.

Investigator initiated studies

- 3,4 DAP in Musk+ MG
- CTS and associated symptoms in hATTR amyloidosis
- Bright tongue sign in Pompe disease
- Spinraza in adult patients with SMA

3,4 DAP in MUSK+MG

CTS and associated symptoms in hATTR amyloidosis
Spinraza in adult patients with SMA

• 10/25 SMA type 2 and type 3 treated
• 3 underwent laminectomy
• 1 developed meningitis
• 2 developed post LP headache
• 1 stopped therapy after 1 year due to lack of benefit
• 1 felt more function in fingers, stronger core muscles and speech
• 8 feel stable

Thank you